UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/870,353	05/30/2001	Yan Wang	020130-000111US	8319

20350 7590 05/26/2004

TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
HUTSON, RICHARD G	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 05/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/870,353	WANG ET AL.	
	Examiner	Art Unit	
	Richard G Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants cancellation of claims 1, 4-8, 11-14 and the amendment of claims 30 and 40, in the paper of 3/2/2004, is acknowledged. Claims and 15-42 are at issue and are present for examination.

Applicants' arguments filed on 3/2/2004, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 15-18 and 22-29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection was stated in the previous office action. In response applicants traverse the rejection on the following basis. Applicants submit that in making the current rejection one should not become confused between the description requirement and the enablement requirement, as the description requirement requires that the inventor understood what his invention was at the time of filing (possession) and the

enablement requirement requires that the public will be taught how to practice the invention after the patent expires.

Applicants submit that in the instant situation, the description based rejection is based entirely by an enablement concern as the examiner has stated that the pending claims fail to establish that the applicants was in possession of the invention because "according to the examiner, the pending claims fail to establish that the applicant was in possession of the invention because there was no SAR data provided to teach those of skill how to make variations of the exemplified species." Applicants have mis-interpreted the basis of the previous rejection. The previous rejection stated:

> "the specification, however, only provides the representative species of Sso7d-delta*Taq*, Sso7d-*Taq*, and *Pfu*-Sso7d encompassed by these claims. There is no disclosure of any particular structure to function/activity relationship in the disclosed species **with respect** to those double-stranded nucleic acid binding domains which are capable of enhancing the processivity of an attached DNA polymerase domain beyond the full-length Sso7d protein."

It was/is not the intent of the instant rejection to state that applicants have not taught "a structure to function/activity relationship in the disclosed species to teach those of skill how to make variations of the exemplified species, but rather applicants have not disclosed a structure to function/activity relationship sufficient for the adequate description of the claimed genus of double-stranded nucleic acid binding domains which are capable of enhancing the processivity of an attached DNA polymerase domain.

In arguing applicants position, applicant refers to the Federal Circuits' decision in *University of California v. Eli Lilly Co.* where the Federal Circuit affirmed the invalidity of the U.C.'s patent claims to any insulin-encoding gene including claims directed to the human insulin gene.

Applicants argue that instant application of a rejection based on a lack of written description is improper because the subject invention is a new use for an old and well-known family of proteins. Applicants submit that in contrast to the U.C. facts, the DNA binding domains of this invention are not a new family of genes, but rather the invention is simply the insightful recognition that processivity of nucleic acid polymerases can be improved by the fusion of the polymerase to non-sequence specific DNA binding domains and both parts of the fusion are known. Applicants submit that there are three major classes of DNA binding proteins identified by the specification and the pending claims are focused on one family, i.e. basic chromosomal proteins from hyperthermophilic archaeabacteria.

Applicants submit that the primary concern of the rejection is that polyclonal antibodies will recognize muteins (man-made amino acid modifications) that are inoperable and that without further information regarding structure and activity one would not know hoe to sort the inoperable from the operable embodiments without undue experimentation.

Further in support of applicants' position applicants have submitted a Rule 132 Declaration by Dr. Vander Horn.

Applicants above arguments are acknowledged, however, not found persuasive to overcome the current rejection. As previously stated, claims 15-18 and 22-29 are directed to all possible proteins comprising two heterologous domains wherein the first domain is any sequence-non-specific-double-stranded nucleic–acid-binding domain wherein said domain specifically binds to any polyclonal antibody generated against Sso7d, joined to any DNA polymerase domain.

Applicants above arguments that applicants invention is simply the recognition that processivity of nucleic acid polymerases can be improved by the fusion of the polymerase to non-sequence specific DNA binding domains is acknowledged, however applicants assertion that both parts of the fusion are known is not persuasive. Applicants interpretation that the "polymerase" language is not similarly rejected as the language referring to the "non-specific double-stranded nucleic acid binding domain" because the structure and function of polymerase are well known is acknowledged. Applicants assertion that as stated by Dr. Vander Horn's Rule 132 Declaration, that the same is true for the "Archea-type DNA binding proteins" is also acknowledged, however applicants claims are not directed to fusions of the "Archea-type DNA binding proteins", but rather to a fusion of a "sequence non-specific double stranded nucleic acid binding protein that specifically binds to polyclonal antibodies generated against Sso7d". It is the genus of the referred to "sequence non-specific double stranded nucleic acid binding protein that specifically binds to polyclonal antibodies generated against Sso7d" that are not adequately described for the reasons previously stated. The structural description a "sequence non-specific double stranded nucleic acid binding protein such

that it merely "specifically binds to polyclonal antibodies generated against Sso7d" is insufficient to adequately describe the claimed genus of fusion proteins.

There is no disclosure of any particular structure to function/activity relationship in the disclosed species with respect to those double-stranded nucleic acid binding domains which are capable of enhancing the processivity of an attached DNA polymerase domain beyond the full-length Sso7d protein. Given this lack of additional representative species as encompassed by the claims, applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 15-29 and 30-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a protein comprising two heterologous domains wherein the first domain is a sequence-non-specific-double-stranded nucleic–acid-binding domain joined to a second domain which is a DNA polymerase domain, wherein said sequence-non-specific-double-stranded nucleic–acid-binding domain is selected from the group consisting of Sso7d or Sac7d, does not reasonably provide enablement for any protein comprising two heterologous domains wherein the first domain is a sequence-non-specific-double-stranded nucleic–acid-

binding domain joined to a second domain which is a DNA polymerase domain, wherein said sequence-non-specific-double-stranded nucleic–acid-binding domain comprises an amino acid sequence that has at least 50% identity to a 50 amino acid subsequence of SEQ ID NO: 2 or said sequence-non-specific-double-stranded nucleic–acid-binding domain comprises an amino acid sequence that has at least 75% identity to the Sac7d sequence set forth in SEQ ID NO: 10. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection was stated in the previous office action. In response to this rejection applicants traverse the rejection and present the Rule 1.132 declaration by Dr. Peter Vander Horn. Applicants traverse the rejection on the basis that the claims 15-29 which recite 50%, 75% and 85% identity to Sso7d and claims 30-42 which recite similar percent identities for Sac7d are enabled in view applicants' parent application, now issued as U.S. Pat. No. 6,627,424, which is drawn to 90% sequence identity, and the reasons stated by Dr. Vander Horn's declaration.

Applicants submit that according to Dr. Vander Horn, a Genbank search readily identifies at least 18 known DNA binding proteins that have amino acid identities of between 98-79% and that this indicated this group of proteins represents an old family tree and that Dr. Vander Horn has created a hybrid protein combining known natural variations to obtain a protein with 76% identity to Sso7d.

Applicants submission that applicants could create a single hybrid protein combining known variations to obtain a protein with 76% identity to Sso7d variant does

not enable the scope of the claimed genus of fusion proteins comprising any sequence-non-specific-double-stranded nucleic–acid-binding domain having a mere 50%, 75% and 85% identity to Sso7d and Sac7d.

Applicants further submit that the use of conservative substitution and SAR data lowers the percent identity to below 60% because in addition to the natural variations between family members, any protein chemist readily understands that conserved substitutions are possible throughout the primary sequences of the prototype proteins. Applicants submit that the combination of all this knowledge permits those of skill to routinely identify species that have less than 60% identity, an example of which is provided by Dr. Vander Horn in section 14 of his declaration.

Applicants further argue that beyond the above referred to objective evidence, applicants submit there exists additional legal precedent which supports the allowance of claims to the scope presently pending. Applicants specifically refer to Application of Herschler, 200 USPQ 711 (CCPA 1979).

Here applicants point out that applicants had discovered that DMSO was useful as a transdermal carrier for physiologically active steroids, and that the description of a single steroid supported a claim to the genus of all steroids. Applicants submit that in a parallel fashion, the instant invention concerns the fusion of a DNA-binding protein to a polymerase to improve processivity and the fact that not all DNA binding proteins are known is an irrelevant truth because you don't need that degree of enablement to allow a claim that does not rely on that element for its patentability, as one of skill would understand that many binding proteins from Archeons, as a genus, are capable of

binding DNA nonspecifically and if provided with a novel protein, one of skill could easily determine with no undue experimentation, whether or not the peptide binds nonspecifically to nucleic acid.

Applicants arguments are acknowledged and have been considered in full but are found nonpersuasive. Applicants are reminded that in making applicants arguments applicants frequently refer to the genus of proteins from Archeons, when the claimed genus is drawn to any non-specific double-stranded nucleic acid binding domain that either a) specifically binds to polyclonal antibodies generated against Ss07d or comprises an amino acid sequence that has at least 50% identity to a 50 amino acid subsequence of SEQ ID NO: 2. While methods to produce variants of a known sequence such as site-specific mutagenesis, random mutagenesis, etc. are well known to the skilled artisan producing variants as claimed by applicants (i.e., having sequence non-specific double-stranded nucleic acid binding activity) requires that one of ordinary skill in the art know or be provided with guidance for the selection of which of the infinite number of variants have the claimed property. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute undue experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification. As previously stated the specification does not establish:: (A) regions of the protein structure which may be modified without

effecting the sequence-non-specific-double-stranded nucleic–acid-binding activity; (B) the general tolerance of the domains to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of said domains with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain function claimed and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable, it would require undue experimentation for one skilled in the art to arrive at the majority of those polypeptides of the claimed genus having the claimed activities.

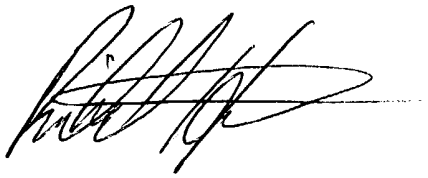
Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any protein comprising two heterologous domains wherein the first domain is a sequence-non-specific-double-stranded nucleic–acid-binding domain joined to a second domain which is a DNA polymerase domain, wherein said sequence-non-specific-double-stranded nucleic–acid-binding domain comprises an amino acid sequence that has at least 50% identity to a 50 amino acid subsequence of SEQ ID NO: 2 or specifically binds to polyclonal antibodies generated against Sso7d, or said sequence-non-specific-double-stranded nucleic–acid-binding domain comprises an amino acid sequence that has at least 75% identity to the Sac7d sequence set forth in SEQ ID NO: 10. The scope of the claims must bear a reasonable

correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgh
5/21/2004